b.) Remarks

Claims 1, 80 and 81 are amended in order to recite the present invention with the specificity required by statute. Additionally, claim 15 is cancelled as superfluous. The subject matter of the amendment may be found in Example 14 and claim 15. Accordingly, no new matter has been added.

Claims 1, 15, 18-21, 23-75 and 80-90 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. In support of the rejection the Examiner states there is no literal support for culturing embryonic stem cells *in vitro*, there is no literal support for culturing cells in the absence of retinoic acid and BMP-4, and there is no literal support for culturing cells in the presence of OP9 or PA6 stroma cells without forming embryoid body. Lastly, the Examiner states literal support that such "is effecting the embryonic stem cell to differentiate into the claimed neural cells cannot be found".

In response, claim 81 has been amended to address the Examiner's concerns. As to the remaining points,

- Examples 1 and 14 show culturing embryonic stem cells *in vitro*.

- specification page 45, lines 1-5 explicitly teaches it is preferable that retinoic acid is not used. Moreover, although the Examiner points out that the feature "in the absence of retinoic acid" is not supported by Examples 1 and 14 such is untrue. Examples 1 and 14 do not utilize retinoic acid in Examples 1 and 14.

- cells that are positive for dopaminergic neuron marker, cholinergic neuron marker, GABAergic neuron marker and serotonergic neuron marker (as recited in

claim 80) were obtained by Example 1. Examples 10 and 11 evidence that such dopaminergic neuron can function as neuron.

• stem cells that are stained by anti-nestin antibody (as recited in claim 81) are obtained by Example 1. Specification page 23, lines 23-29 confirm that neural stem cells can be confirmed by staining by anti-nestin antibody.

Accordingly, this rejection is overcome.

Claims 1, 15, 18-21, 23-75 and 80-90 are rejected under 35 U.S.C. §112, first paragraph for the reasons discussed at pages 4-10. According to the Examiner, the conditions applicable for controlling the differentiation of mouse embryonic stem cells are not applicable to human embryonic stem cells. This is a repeat of a previously-withdrawn rejection.

In this regard, the Examiner may recall that in the Office Action dated January 16, 2003, it was asserted only treating mouse ES cells was enabled. In response, Applicants submitted *PNAS*, Vol. 99 (2002) 1580 and pointed out that even in monkey ES cells, differentiation of dopaminergic neuron is induced by the method of the present invention. If the Examiner is now aware of information why such showing is irrelevant, she is respectfully requested to provide a suitable affidavit under MPEP §2144.03.

Moreover, to the extent the Examiner may be no longer persuaded by this argument, *Cell*, Vol. 131, No. 5 (2007) 861-72 (copy attached) shows the method of the present invention can be applied to human ES cells. See the first sentence in right column on page 864 ("human iPS cells could be induced by reported methods for hES cells")

followed by description of the experiment doing so (page 864, right column, line 3, et seq. and Figure 6).

Accordingly, this rejection is overcome as well.

Claims 1, 23, 81 and 82-87 are rejected under 35 U.S.C. §103(a) as being obvious over Nakano (*Science*, Vol. 265 (1994) 1090-1101) in view of Samarut (U.S. Patent No. 6,114,168).

This rejection is respectfully traversed. However, in view of the fact that none of claims 15, 18-21, 24, 74, 75, 80, 81 or 88-90 is rejected over the prior art. Applicants have above amended claims 1, 80 and 81 to recite the subject matter of claim 15 in order to expedite prosecution. Accordingly, this rejection is mooted.

In view of the above amendments and remarks, Applicants submit that all of the Examiner's concerns are now overcome and the claims are now in allowable condition. Accordingly, reconsideration and allowance of this application is earnestly solicited

Claims 1, 18-21, 23, 24, 74, 75 and 80-90 remain presented for continued prosecution.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,

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